TRANSMITTAL #: 80
DATE: 01/14/2005
TRICARE CHANGE #: C-11

CHAMPVA POLICY MANUAL

CHAPTER: 2
SECTION: 31.10
TITLE: HIGH DOSE CHEMOTHERAPY AND STEM CELL TRANSPLANTATION

AUTHORITY: 38 CFR 17.270(a), 17.272(a)(1)(4)(13)(14)(59), and 17.273

RELATED AUTHORITY: 32 CFR 199.4(e)(5) and (g)(15)

I. EFFECTIVE DATE

A. November 1, 1983, for HDC (High Dose Chemotherapy) with allogeneic bone marrow transplants using related donors.

B. May 1, 1987, for HDC with ABMT (Autologous Bone Marrow Transplant) or PSCT (Peripheral Stem Cell Therapy) for Hodgkin's disease, non-Hodgkin's lymphoma and neuroblastoma.

C. November 1, 1987, for HDC with ABMT or PSCT for acute lymphocytic and non-lymphocytic leukemias.

D. July 1, 1989, for HDC with allogeneic bone marrow transplants using unrelated donors.

E. January 1, 1994, for HDC with ABMT or PSCT for chronic myelogenous leukemia.

F. January 1, 1994, for HDC with ABMT and PSCT for Wilm's tumor.

G. January 1, 1995, for ABMT for hypereosinophilic syndrome.

H. January 1, 1995, for allogeneic umbilical cord blood transplants.

I. June 1, 1995, for allogeneic bone marrow transplants for Chediak-Higashi syndrome.

J. January 1, 1996, for allogeneic bone marrow transplants using related 3-antigen mismatch donors for patients with undifferentiated leukemia, CML (Chronic Myelogenous Leukemia), aplastic anemia, ALL (Acute Lymphocytic Leukemia) or AML (Acute Myelogenous Leukemia).

K. January 1, 1996, for HDC with ABMT or PSCT for Waldenstrom's macroglobulinemia.

L. January 1, 1996, for HDC with allogeneic bone marrow transplants for multiple myelona.

M. July 11, 1996, for HDC with ABMT or PSCT for multiple myeloma.

N. October 1, 1996, for HDC with ABMT or PSCT for AL (Amyloid Light)-chain amyloidosis.

O. January 1, 1997, for HDC with ABMT or PSCT for follicular lymphoma.

P. January 1, 1997, for HDC with ABMT or PSCT for non-Hodgkin's lymphoma in first complete remission.

Q. May 1, 1997, for HDC with ABMT or PSCT for trilateral retinoblastoma/ pineoblastoma.

R. November 28, 1997, for HDC with ABMT or PSCT for Hodgkin's disease in second or third remission.

S. January 1, 1998, for allogeneic peripheral stem cell transplantation.

T. January 1, 1998, for HDC with ABMT or PSCT for osteosarcoma (osteogenic sarcoma).

U. July 1, 1999, for HDC with ABMT or PSCT for germ cell tumors in a second or subsequent relapse.

V. January 24, 2002, for allogeneic stem cell transplant for Hodgkin's disease.

W. September 2, 2002, for agnogenic myeloid metaplasia (myelofibrosis).

X. June 1, 2003, for Langerhans Cell Histiocytosis, refractory to conventional treatment.

II. PROCEDURE CODE(S)

38205-38206, 38230-38241, 86812-86822, and 88240-88241

III. DESCRIPTION

A. HDC (High Dose Chemotherapy) as the use of cytotoxic therapeutic agents (that are otherwise approved for general use in humans) by the FDA (Food and Drug Administration) in dosages and/or frequencies of dosage that exceed the FDA labeling

for the agent. HDC is generally considered when conventional regimens of chemo-therapeutic agents have failed to arrest disease progression. One of the major adverse effects of HDC when bone marrow suppression occurs, it can be a lethal process.

B. Stem cells are multipotential, blood-cell producing agents important in immune defenses against disease. Stem cell "transplantation" or "rescue" is defined as a technique for collecting stem cells from a donor (either from the bone marrow or from the bloodstream), preparing and storing the collected stem cells, then reinfusing the prepared stem cells into the bloodstream of a patient in the treatment of oncologic, hematologic or lymphoproliferative disease with curative potential. The goal of stem cell "transplantation" or "rescue" is to reverse the bone marrow suppression caused by either HDC or by a primary bone marrow disease process, that is, aplastic anemia.

C. There are five general types of stem cell “transplantation” or “rescue”:

1. Allogeneic bone marrow transplantation, where stem cells from a histocompatible donor (other than the patient) are harvested from the bone marrow, then later infused into the bloodstream of the patient. With Allogeneic bone marrow transplantation, the patient may have either a related or unrelated donor who has the same or closely matched HLA (Human Leukocyte Antigen) typing necessary for successful transplantation.

2. Allogeneic PSCT (Allogeneic Peripheral Stem Cell Transplantation) where stem cells are harvested from the bloodstream of a histocompatible donor (other than the patient) then later infused into the bloodstream of the patient.

3. ABMT, where the patient is both donor and recipient of stem cells harvested from the bone marrow.

4. Autologous PSCT (Peripheral Stem Cell Transplantation), where the patient is both donor and recipient of stem cells harvested from the bloodstream using the apheresis process.

5. UCBT (Umbilical Cord Blood Stem Cell Transplantation), where stem cells are harvested from the umbilical cord and placenta, then later infused into the bloodstream of the patient.

IV. POLICY

A. Benefits are allowed for HDC with ABMT or Augologous PSCT, Allogeneic bone marrow transplants, Allogeneic PSCT (with or without HDC), and Allogeneic UCBT (with or without HDC), for the following indications. The list is not all-inclusive. Other indications are covered when documented by reliable evidence as safe, effective, and comparable or superior to standard care (proven).

1. Acute lymphocytic or nonlymphocytic leukemias, such as, myelocytic, myelogenous, myeloblastic, or myelomonoblastic, chronic myelogenous leukemia, or preleukemic syndromes.

2. Amyloid light-chain amyloidosis.

3. Chronic myelogenous leukemia.

4. Germ cell tumors in a second or subsequent relapse.

5. Glioblastoma (a malignant, fast growing tumor) multiforme.

6. Gliofibromas (also known as desmoplastic astrocytoma and desmoplastic glioblastoma).

7. Hodgkin's disease when:

a. Conventional dose chemotherapy has failed; or

b. The patient has relapsed following a course of radiation therapy, and also failed at least one course of conventional dose chemotherapy subsequent to the failed radiation therapy; and

c. The patient is in second or third complete remission.

8. Multiple myeloma. Tandem autologous stem cell transplantation is covered for the treatment of multiple myeloma.

9. Neuroblastoma, Stage III or IV, when the patient is one for who further treatment with a conventional dose therapy is not likely to achieve a durable remission.

10. Non-Hodgkin's lymphoma, follicular, intermediate or high-grade, when:

a. Conventional dose chemotherapy has failed; or

b. The patient has relapsed following a course of radiation therapy; or

c. The patient is in their first complete remission with risk factors for relapse.

Note: For purposes of coverage, mantle cell lymphomas will be considered as intermediate grade, non-Hodgkin's lymphomas.

11. Osteosarcoma (osteogenic sarcoma).

12. Posterior fossa teratoid brain tumors.

13. PNET (Primitive Neuroectodermal Tumors)/Ewing's Sarcoma.

14. Rhabdomyosarcoma and undifferentiated sarcomas.

15. Testicular cancer (germ cell) for patients with refractory relapsed disease who have failed standard dose salvage regimen.

16. Trilateral retinoblastoma/pineoblastoma.

17. Waldenstrom's macroglobulinemia.

18. Wilm's tumor.

B. Allogeneic bone marrow transplants or allogeneic PSCT, with or without HDC is covered for the indications listed below when either a related or unrelated donor is used. This list is of indications is not all-inclusive. Other indications are covered when documented by reliable evidence as safe, effective, and comparable or superior to standard care (proven).

1. Aplastic anemia.

2. Anogeneic myeloid metaplasia (myelofibrosis).

3. Acute lymphocytic or nonlymphocytic leukemias, such as, myelocytic, myelogenous, myeloblastic, myelomonoblastic, chronic myelogenous leukemia, or preleukemic syndrome.

4. Chediak-Higashi Syndrome.

5. CLL (Chronic Lymphocytic Leukemia) when previous therapy has failed or when the CCL is refractory to conventional therapy.

6. CGL (Chronic Granulocytic Leukemia).

7. Chronic myelogenous leukemia.

8. Congenital amegakaryocytic thrombocytopenia.

9. Congenital mucopolysaccharidoses (Hunter's, Hrler's, etc.).

10. Hypereosinophilic syndrome.

11. Hodgkin's lymphoma for Stage III or IV A or B patients who are either in relapse, or refractory to primary chemotherapy.

12. Follicular non-Hodgkin's lymphoma for patients who have failed primary therapy.

13. Infantile malignant osteopetrosis (Albers-Schonberg syndrome or marble bone disease).

14. Intermediate and high grade lymphoma.

15. Kostmann's Syndrome (severe infantile agranulocytosis).

16. Langerhans Cell Histiocytosis, refractory to conventional treatment.

17. Leukocyte adhesion deficiencies.

18. Metachromatic leukodystrophy.

19. Multiple myeloma when HCD with ABMT or Autologous PSCT has failed.

20. Mucolipoidoses (Gaugher's, metachromic leukodystrophy, etc.).

21. Myelodysplasia/myelofibrosis for patients with refractory anemia (idiopathic, or secondary to drug or toxin exposure), who have an HLA-identical donor. Patients must have one or more of the following:

a. excess blasts or excess blasts in transformation,

b. chronic myelomonocytic leukemia, or

c. increasing blast counts or ringed sideroblasts with at least one of the following: neutropenia, thrombocytopenia or chromosomal abnormalities.

22. Myeloproliferative/dysplastic syndromes.

23. Non-Hodgkin's lymphoma when:

a. Stage III or IV A or B, intermediate and high grade non-Hodgkin's lymphoma in second or subsequent clinical remission.

b. Stage IV A or B, high-grade non-Hodgkin's lymphoma with a lymphoma mass over 10 cm and with more than one involved extranodal site, in first clinical remission, because these patients have such a high likelihood of recurrence.

24. Severe combined immunodeficiency, such as, adenosine deaminase deficiency and idiopathic deficiencies.

a. Partially matched-related donor stem cell transplantation (without regard for the number of mismatched antigens in determining histocompatibilitiy) in the treatment of Bare Lymphocyte Syndrome.

b. Unrelated donor and/or related donor (without regard for mismatched antigens) with or without T-cell lymphocyte depletion in the treatment of FEL (Familial Erythrophagocytic Lymphohistiocytosis);generalized lymphohistiocytic infiltration; familial lymphohistiocytosis, familial reticuloendotheliosis; and FHL (Familial Hemophagocytic Lymphhistiocytosis); for patients whose medical records document failure of conventional therapy (etoposide; corticosteroids; intrathecal methotrexate; and cranial irradiation).

c. Partially matched-related donor stem cell transplantation (without regard for the number of mismatched antigens) in the treatment of X-Linked SCID (Severe Combined Immunodeficiency Syndrome). Amegakaryocytic thromboyctopenia.

25. Sickle cell disease.

26. Thalassemia major.

27. Wiskott-Aldrich Syndrome.

28. X-linked hyper-IgM Syndrome.

C. Unirradiated donor lymphocyte infusion (donor buffy coat infusion, donor leukocyte infusion or donor monomuclear cell infusion) is covered for patients with chronic myelogenous leukemia, who relapse following their first or subsequent course of HDC with allogeneic bone marrow transplants. The medical record must document that the patient:

1. is in relapse following an adequate trial of HDC with allogeneic bone marrow transplants or chronic myelogenous leukemia, and

2. qualified (or would have qualified) for authorization for HDC with allogeneic bone marrow transplants according to the provisions set forth in this policy.

D. Allogeneic UCBT, with or without HDC, is covered in the treatment of the following disease processes when either a related or unrelated donor is used. This list of conditions is not all-inclusive, those conditions for which this procedure can be documented as medically necessary, appropriate and the standard of care may also be covered.

1. Acute lymphocytic or non-lymphocytic leukemias.

2. Adrenoleukodystrophy.

3. Aplastic anemia.

4. Blackfan-Diamond anemia.

5. Chronic myelogenous leukemia.

6. Congenital amegakaryocytic thrombocytopenia.

7. Fanconi anemia.

8. Globoid cell leukodystrophy.

9. Hurler syndrome.

10. Hunter syndrome.

11. Infantile malignant osteopetrosis.

12. Intermediate and high grade non-Hodgkin's Lymphoma.

13. Kostmann's syndrome.

14. Lesh-Nyhan disease.

15. Myelodysplastic syndrome.

16. Neuroblastoma.

17. Non-Hodgkin’s lymphoma.

18. Severe combined immunodeficiency.

19. Sickle cell anemia.

20. Thalassemia major.

21. Wiskott-Aldrich syndrome.

22. X-linked hyper-IgM Syndrome

23. X-linked lymphroproliferative syndrome.

24. Langerhans Cell Histiocytosis, refractory to conventional treatment.

E. Syngeneic (identical twin donor) stem cell transplantation is covered for the treatment of Hodgkin's disease.

F. Unrelated Donor. In those allogeneic stem cell transplantation cases in which it has been established that a related donor is not possible, and when the only alternative is an unrelated donor, benefits may be extended only under the following conditions:

1. The patient must use the NMDP (National Marrow Donor Program) for donor searches. (The NMDP is located in Minneapolis, Minnesota, 1-800-654-1247, and is available to anyone needing assistance in locating a suitable donor for unrelated allogeneic bone marrow transplantation). Donor searches through foreign registries must first be initiated or coordinated through NMDP. Prior to using NMDP services, pre-authorization for services must be obtained from the HAC.

2. Donor matching must meet the criteria established by the NMDP for identical and mis-matched typing.

3. Requests for a donor search must be initiated and coordinated through the NMDP, and the transplant must be performed at one of its NMDP certified centers.

G. Donor Search. CHAMPVA will reimburse costs for donor searches only when the search has been initiated and coordinated by the NMDP.

1. Charges for donor searches must be fully itemized and billed by the transplant center and will be cost shared in accordance with established reimbursement guidelines for outpatient diagnostic testing.

2. Donor search costs may be billed at any time. There is no limit on how many searches a transplant center may request from the search printout.

H. Histocompatibility criteria. In the cases where related donor matches are not perfect, e.g., the histocompatibility is less than an identical antigen match; the same criteria and standards for typing mismatched unrelated donors must be used.

1. For the purposes of the National Donor Program and CHAMPVA coverage, the greatest degree of incompatibility allowed between donor or recipient (for either related or unrelated donors) is a single antigen mismatch at the A, B, or Dr. locus except for:

a. Patients with undifferentiated leukemia, chronic myelogenous leukemia, aplastic anermia, acute lymphocytic or acute myelogenous leukemia, when histocompatible related or unrelated donors are not available, 3-antigen mismatch is allowed for related donors.

b. For patients under 18-years of age with a relapsed leukemia, when histocompatible related or unrelated donors are not available, parental CD34++ stem cell transplantation with 2-3-antigen mismatch is allowed.

2. Donor searches accomplished through foreign registries must meet the same typing criteria as established by the NMDP.

3. DNA-HLA tissue typing to determine histocompatibility is covered.

I. Benefits prior to stem cell reinfusion. Benefits will not be allowed for stem cell harvesting and/or cryopreservation and umbilical cord blood stem cell harvesting and/or cryopreservation until the stem cell reinfusion has been completed. In the event that the patient expires prior to the stem cell reinfusion being completed, benefits for the harvesting may be allowed.

J. Hepatitis B. Benefits are allowed for Hepatitis B and pneumococcal vaccines for patients undergoing transplantation.

K. Umbilical Cord Blood Preparation and Storage. Charges for stem cell and umbilical cord blood preparation and storage shall be billed through the transplantation facility in the name of the CHAMPVA patient.

L. Umbilical Cord Blood Bank. Charges for the umbilical cord blood bank may be allowed only for patients who have undergone a covered transplant.

V. POLICY CONSIDERATIONS

A. Pre-authorization and retrospective authorization for HDC with Allogeneic bone marrow transplants or allogeneic PSCT, or HDC with ABMT and Autologous PSCT, or UCBT with HDC must meet the following two criteria:

1. The patient meets (or as of the date of transplantation, would have met) patient selection criteria.

2. The transplant facility is (or as of the date of transplantation would have been) Medicare, TRICARE, or VA approved.

B. In those cases where the beneficiary fails to obtain pre-authorization, benefits may be extended if the services or supplies otherwise would qualify for benefits but for the failure to obtain pre-authorization. If pre-authorization is not received, the HAC will review the claim to determine whether the beneficiary's condition meets the clinical criteria for the transplantation.

C. Claims for services and supplies related to the HDC and transplant for beneficiaries under the age of 18 will be reimbursed based on the billed charges. Claims for HDC and transplant for adult patients, 18-years and older, will be reimbursed under the DRG (Diagnostic Related Group) payment system. Outpatient institutional facility charges will be paid as billed. Professional services are reimbursed under the CMAC (CHAMPUS Maximum Allowable Charge) methodology.

D. Donor costs are payable under the conditions as outlined within Chapter 2, Section 31.1, *Donor Costs*.

E. Air ambulance may be cost shared when determined to be medically necessary (see Chapter 2, Section 32.1, *Ambulance Service*).

VI. EXCEPTIONS

If the patient otherwise meets the coverage criteria for HDC with ABMT as listed in POLICY above, harvesting of the required stem cells by apheresis from peripheral blood, that is, PSCT, rather than bone marrow, may be allowed.

VII. EXCLUSIONS

A. Administration of an unproven immunosuppressant drug that is not FDA approved.

B. Allogeneic bone marrow transplant or PSCT with HDC for treatment of multiple myeloma, except as indicated in policy.

C. Allogeneic bone marrow transplantation for neuroblastoma.

D. Allogeneic PSCT for non-Hodgkin's lymphoma,

except as indicated in Policy.

E. Allogeneic stem cell transplant for:

1. CLL (Chronic Lymphoma Leukemia), except as indicated in policy;

2. ovarian cancer;

3. SLL (Small Lymphocytic Lymphoma);

4. solid tumors; and

5. polycythemia vera.

F. Allogeneic bone marrow transplantation for treatment of low grade non-Hodgkin's lymphoma.

G. Allogeneic donor bone marrow transplantation (infusion) performed with or after organ transplants for the purpose of increasing tolerance of the organ transplant.

H. Autologous umbilical cord transplantation therapy.

I. Donor lymphocyte infusion (donor buffy coat infusion, donor leukocyte infusion, and donor mononuclear infusion) if not specifically listed as covered above.

J. HDC with Autologous ABMT or Autologous PSCT, Allogeneic bone marrow transplantation or Allogeneic PSCT, or Allogeneic UCBT, with or without HDC, if the patient has a concurrent condition (other existing illness) that would jeopardize the achievement of successful transplantation.

K. HDC with ABMT or Autologous PSCT for the following:

1. Desmoplastic small round-cell tumor.

2. Non-metastatic breast cancer.

3. Yolk sac tumor (endodermal sinus tumor).

L. HDC with allogeneic bone marrow transplantation is not a benefit for treatment of Waldenstrom's macroglobulinemia.

M. HDC with allogeneic bone marrow transplatation for the treatment of Hodgkin's disease. This does not include syngeneic stem cell transplantation which is covered for the treatment of Hodgkin's disease.

N. HDC with Allogeneic PSCT for the treatment of cold agglutinin disease.

O. HDC with or without ABMT, HDC with or without Autologous PSCT, or HDC with or without allogeneic bone marrow transplantation, if not specifically listed as covered in paragraphs A and B under POLICY above.

P. HDC with stem cell rescue for the following:

1. epithelial ovarian cancer, and

2. testicular cancer, except as indicated in policy.

Q. In-vitro stem cell processing (stem cell assay or purging).

R. Reduced intensity transplants (non-myeloablative allogeneic stem cell transplants, mini transplants, transplant lite) for renal cancer and other solid tumors of solid tissues or organs.

S. Salvage HDC/AlloSCS (High Dose Chemotherapy/Allogeneic Stem Cell Support) after HDC/AuSCS (High Dose Chemotherapy/Autologous Stem Cell Support) for patients with recurrent neuroblastoma, breast cancer, germ cell tumors in relapse, or any other solid tumor.

T. Salvage HDC/AlloSCS for relapse of incomplete remission after HDC/AuSCS for patients with multiple myeloma, non-Hodgkin's lymphoma, Hodgkin's lymphoma, acute myeloblastic leukemia and acute lymphoblastic leukemia.

U. Pre- or post- transplant nonmedical expenses, that is, out-of-hospital living expenses, to include, hotel, meals, privately owned vehicle for the beneficiary or family members. [38 CFR 17.272(a)(4)]

V. Services/supplies provided at no cost or if the beneficiary (or sponsor) has no legal obligation to pay. This includes expenses or charges that are waived by the transplantation center. [38 CFR 17.272(a)(14)]

W. Services, supplies or devices, even those used in lieu of the transplantation, when determined to be related or integral to an experimental/investigational (unproven) procedure. [38 CFR 17.272(a)(1)]

X. Services and supplies not provided in accordance with applicable program criteria (i.e., part of a grant, or research program; unproven procedure). [38 CFR 17.272(a)(13)(14)]

Y. Transportation of a donor living or cadaver. [38 CFR 17.272(a)(59)]

END OF POLICY